REMARKS/ARGUMENTS

Claims 1-46 are pending in this application and presented for examination. Claims 1 and 29 (withdrawn) have been amended to more particularly point out and distinctly claim the subject matter. Claims 1-3, 18, 19, 22, 23 and 26 were examined in this Office Action. No new matter has been introduced with the foregoing claim amendments. Reconsideration is respectfully requested in view of the remarks below.

I. REJECTION UNDER 35 U.S.C. § 102(b)

The Examiner has maintained the rejection of claims 1-3, 18-19 and 26 under 35 U.S.C. § 102(b) as allegedly being anticipated by Yao *et al.*, *Genes to Cells* (1996) 1 101-113 ("Yao *et al.*"). To the extent the rejection is applicable to the amended set of claims, Applicant respectfully traverses the rejection.

As amended, claim 1 now recites:

> A polymerase-nucleic acid complex, said polymerase-nucleic acid complex comprising: a target nucleic acid and a nucleic acid polymerase, wherein said polymerase has an attachment complex comprising at least one anchor covalently attached thereto, said at least one anchor having a modified amino acid, which attachment complex irreversibly associates said target nucleic acid with said polymerase to increase the processivity index.

In the Office Action, the Examiner stated that "Applicants seem to argue that the attachment complex must be covalently bound to the polymerase: no such limitation is present in the claims...".

In order to expedite prosecution of this application, Applicant has now amended the claim to make it clear that the anchor is covalently attached to the polymerase. In the present claims, the attachment complex comprises at least one anchor which irreversibly associates the target nucleic acid with the polymerase. In other words, the polymerase attachment complex comprises a covalently attached anchor, wherein the anchor has a modified amino acid. Thus, in order to accommodate the covalent anchor, the polymerase itself must also be modified to have

an attachment complex, which complex has at least one anchor. The at least one anchor has a modified amino acid to make the covalent attachment to the polymerase.

Further, the attachment complex, which comprises at least one anchor, irreversibly associates the target nucleic acid with the polymerase to increase the processivity index. As discussed in the specification at paragraphs 41-42:

> In certain instances, the at least one anchor entraps the target nucleic acid such as by folding back on itself. In other instances, the anchors of the present invention are useful for also attaching a topological tether to the polymerase, or for example, attaching the PNAC to a substrate. In other embodiments, the anchor affixes the PNAC to a support, with or without a topological tether. In certain other embodiments, the polymerase-nucleic complex comprises a topological tether bound to at least two anchors.
>
> As shown in Figure 1B, an anchor 130 can further comprise other functionalities such as a first member 135 of a first binding pair. A second anchor 140 has a first member 145 of a second binding pair. As shown in Figure 1C, in certain instances, a topological tether is formed when the first members 135, 145 are joined by a common member 148. Alternatively, a topological tether can be formed when the first members 135, 145 are each joined directly to a support (not shown).

This "attachment complex," which comprises at least one covalently attached anchor to the polymerase is one distinguishing feature from all of the references that the Examiner has cited. The attachment complex is a patentably distinct feature. Various embodiments of the attachment complex are shown in Figure 1. Moreover, unlike the cited reference, a covalent modification is responsible in-part for increasing the processivity index.

Yao *et al.* in no way teach a covalently attached anchor as is currently claimed. In Yao *et al.*, the polymerases are wild-type polymerases with a sliding clamp and no modification to accommodate an anchor. In fact, the polymerases of Yao *et al.* do not possess an anchor at all. Further, Yao *et al.* do not teach an irreversible association between the target nucleic acid with the polymerase. Yao *et al.* teach a strategy of "clamp recycling." In this regard, the Examiner's attention is respectfully directed to page 110, left column of Yao *et al.* wherein it states:

> This rapid **cycling off and on the DNA** is a process that would conceptually be hindered by too tight a grip on the DNA such as incurred by a protein ring. The mechanism for this rapid polymerase cycling has been elucidated in *E coli* and T4 phage systems. The DNA polymerase is tightly held to the sliding clamp during chain extension, but upon completing a template the polymerase rapidly dissociates from its clamp. (citations). [Emphasis added].
>
> Further down the same column it states:
>
> The observed stability of PCNA clamps on DNA suggests that clamp **recycling may be an active process** in eukaryotes as well. [Emphasis added].

The clamps in Yao *et al.* recycle. A skilled person would understand that recycling is NOT an association, which is incapable of being reversed as is currently taught and claimed. As each and every element is not found in the cited reference, the claims are not anticipated. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection and send this application to issue.

II. REJECTION UNDER 35 U.S.C. § 102(a)

The Examiner has maintained the rejection of claims 1-3, 18-19 and 26 under 35 U.S.C. § 102(a) as allegedly being anticipated by Motz *et al.* In view of the amended set of claims, Applicant respectfully traverses the rejection.

Again, Applicant has amended the claims to make it clear that the anchor is covalently attached to the polymerase. In the present claims, the attachment complex comprises at least one anchor which irreversibly associates the target nucleic acid with the polymerase. In other words, the polymerase attachment complex comprises a covalently attached anchor. Thus, in order to accommodate the covalent anchor, the polymerase itself must also be modified to have an attachment complex. Moreover, the at least one anchor has a modified amino acid to make the covalent attachment to the polymerase. This "attachment complex," which comprises

at least one covalently attached anchor to the polymerase is a distinguishing feature over Motz *et al.* Unlike the cited reference, a covalent modification is responsible in-part for increasing the processivity index.

Although Motz *et al.* appears to be silent on the point, there is no reason to believe that the PCNA from *A. fulgidus* is any different from other members of the sliding clamp family of proteins. As such, clamp recycling occurs in Motz *et al.* as in Yao *et al.*

Motz *et al.* in no way teach a covalently attached anchor as is currently claimed. In Motz *et al.* the polymerases are wild type polymerases with a sliding clamp and no modification to accommodate an anchor. In fact, the polymerases of Motz *et al.* do not possess an anchor at all. Further, Motz *et al.* do not teach an irreversible association between the target nucleic acid with the polymerase.

A skilled person would understand that recycling is NOT an association, which is incapable of being reversed as is currently claimed. As each and every element is not found in the cited reference, the claims are not anticipated. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection and send this application to issue.

III. FIRST REJECTION UNDER 35 U.S.C. § 103(a)

The Examiner has rejected claims 19 and 22 under 35 U.S.C. § 103(a) as allegedly being obvious over Motz *et al.* and U.S. Patent No. 5,198,543 ("Blanco *et al.*"). To the extent the rejection is applicable to the amended set of claims, Applicant respectfully traverses the rejection.

This "attachment complex," which comprises at least one covalently attached anchor to the polymerase is a distinguishing feature over Motz *et al.* Blanco *et al.* do not supply the deficiencies of the primary reference. Blanco *et al.* do not teach or even suggest an attachment complex, nor a covalently attached anchor. Blanco *et al.* teach a modified ϕ29 polymerase with a modified exonuclease activity.

Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection and send this application to issue.

IV. SECOND REJECTION UNDER 35 U.S.C. § 103(a)

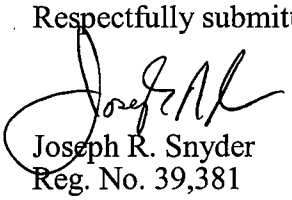
The Examiner has rejected claim 23 as allegedly being obvious over U.S. Patent No. 6,255,083 ("Williams") and Motz *et al.* To the extent that the rejection is applicable to the amended set of claims, Applicant respectfully traverses the rejection.

This "attachment complex," which comprises at least one covalently attached anchor to the polymerase is a distinguishing feature over Williams. Motz *et al.* do not supply the deficiencies of the primary reference. Motz *et al.* in no way teach a covalently attached anchor as is currently claimed. In Motz *et al.* the polymerases are wild type polymerases with a sliding clamp and no modification to accommodate an anchor. In fact, the polymerases of Motz *et al.* do not possess an anchor at all. Further, Motz *et al.* do not teach an irreversible association between the target nucleic acid with the polymerase. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection and send this application to issue.

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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